REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 16-21 will be pending in the application subsequent to entry of this Amendment.

Claim for Benefit of Priority

As a preliminary matter, the Official Actions do not acknowledge receipt of applicants' claim for benefit of priority nor do they acknowledge receipt of certified copies of the priority documents received during this national stage application from the International Bureau. Certified copies were indeed filed during international processing and attached is a Notification from the International Bureau demonstrating this. The examiner is requested to acknowledge both applicants' claim for benefit of priority and also receipt of the two certified copies as indicated on the Filing Receipt of this application in order to complete claim for benefit of priority.

Restriction Requirement/Claim Amendments

Claims directed to non-elected subject matter have been canceled, this action being taken without disclaimer or prejudice to the subject matter of any of these withdrawn and now canceled claims.

The claims have been amended in order to more particularly point out and distinctly claim that which applicants regard as their invention and to attend to formalities issues noted on pages 3 and 4 of the current Official Action. A new title has already been supplied and a new Abstract has been provided.

Basis for the Claim Amendments

Claim 16 is based on pending claim 3.

Basis for claim 17 can be found on page 6, lines 2 and 3.

Basis for claim 18 can be found on page 5, lines 5-7.

Claims 19 and 20 are based on page 6, lines 6 and 7 and page 2, lines 14-16, respectively.

Claim 21 is a combination of claims 16, 17, 19 and 20.

Novelty (35 USC 102(b))

Claims 1 – 3 were rejected as being anticipated by Reinhartz et al EP 0 418 113. It is submitted that new claim 16 is not anticipated by the Reinhartz et al patent.

Reinhartz et al. mentions the Delvotest® in the description of the background of the invention as an example of a biological assay for detecting antibiotics in milk that was commercially available in 1990, the time of Reinhartz's filing (*see* page 2, lines 16 and 17). According to Reinhartz et al. a disadvantage of biological assays of the prior art is their long duration which lead to operational difficulties, especially within the dairy industry (*see* page 2, lines 30 and 31).

Reinhartz et al. further disclose that they have provided an assay that solves the problem associated with the prior art assays for it is rapid and sensitive and can detect antibiotics within 30 minutes or less (*see* page 2, lines 42-47). According to Reinhartz et al. the speed and sensitivity of their assay results from the inventive combination and exploitation of two principles:

a) generation of the highest possible signal from the biological system, and

b) sensitization of the bacteria to the antibacterial compounds to be detected by subjecting them to stresses which relate to the mechanism of action of the antibiotic and/or by selecting a signal generating metabolic system which is affected by the antibiotic (*see* page 2, line 48 – page 3, line 12).

In an embodiment of the invention of Reinhartz et al. the biological assay comprises the steps of (*see* page 3, lines 13-37):

1. cultivating a viable bacterial cell suspension in a suitable growth medium,
2. adding the suspension to the specimen suspected to have the antibacterial compound and to a control specimen known not to contain the antibacterial compound and adding a mixture of yeast extract and tryptose to the obtained mixture,
3. incubating the mixture for a period of up to 30 minutes,
4. diluting the mixture with an aqueous solution containing glucose and a tetrazolium salt, preferably MTT at a specific concentration; alternative signal generating systems that can be used within the biological assay of Reinhartz et al. are: (i) a mixture of glucose and a pH-indicator e.g. Bromocresol purple or Bromthymol blue; (ii) determining ATP inside or outside the bacterial cells, or (iii) other signal generating systems indicating viability, metabolic activity or membrane integrity, and

5. comparing the result obtained in step 4 of the control with that of the test specimen.

Consequently, Reinhartz et al. discloses to a person skilled in the art nothing more than that a mixture of glucose and a pH-indicator, e.g. Bromocresol purple or Bromthymol blue, can be used as an alternative signal generating system within the specific assay described by Reinhartz et al. Reinhartz et al. only mention the use of Bromthymol blue in combination with their newly found rapid and sensitive biological assay. They do not disclose that the alternative signal generating system should and can be used in connection with an assay described in the prior art, let alone that it should or can be used within the Delvotest®.

In view of the novelty of new claim 16 over Reinhartz et al, it is submitted that new claims 17-20 being dependent on claim 16 are also novel over Reinhartz et al.

Furthermore for sake or argumentation only, it is submitted that the use of Bromthymol blue as a pH indicator in the biological assay as claimed in claims 17-21 is nonobvious over Reinhartz et al. If a person skilled in the art would have felt the need for substituting the indicator in the Delvotest® assay, which is however disputed, he would have chosen for a redox-indicator and not a pH-indicator such as Bromthymol blue on the basis of Reinhartz et al. Reinhartz et al. clearly prefer a redox-indicator, e.g. a tetrazolium salt such as MTT, as an indicator over a pH-indicator (*see* page 3, lines 24-27). MTT has successfully been used in all examples of Reinhartz et al. and even considerable effort has been put into development of methods for visual or instrumental determination of MTT dye (*see* Example 3 on page 5 and 6), which is a further indication that a person skilled in the art, if he would have felt the need to change something in the Delvotest®, would have chosen to exchange the indicator used within the Delvotest® for a redox-indicator such as MTT.

Surprisingly, the present invention now demonstrates that the application of Bromthymol blue as an indicator in a test system for determination of the presence of an antibiotic in a fluid leads to an unexpected advantageous increase in sensitivity (which can amount up to 100%) for antibiotics compared to test systems in which commonly used indicators such as Bromocresol Purple are being used (*see* page 2, lines 14-18 and Examples 1-4 on pages 11-13 of the application as filed). Additionally, it has been found that the use of Bromthymol Blue as an indicator results in an improved visual contrast when comparing positive and negative samples.

This greatly facilitates accurate visual evaluation of test results (*see* page 2, lines 19-21 of the application as filed).

In view of the above argumentation, nonobviousness should be acknowledged for claims 16-21.

Lack of enablement (35 USC 112, first paragraph)

In view of the set of amended claims, this objection is rendered moot.

Indefiniteness (35 USC 112, second paragraph)

The term "at least one substance that provides a solid state" should not be rejected as being indefinite. On page 6, lines 2-5 of the specification a clear explanation of the term is given. Furthermore, examples of suitable substances that provide a solid state are given on page 4, line 30 – page 5, line 2 of the specification. Claims are read and understood in light of the specification and in doing so the skilled reader would fully understand the term.

Further issues put forward by the Examiner with regard to indefiniteness are rendered moot by amending the claims.

Reconsideration and favorable action are solicited. Should the examiner require further information, please advise the undersigned.

Respectfully submitted,

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PATENT COOPERATION TREATY

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NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

Date of mailing (day/month/year) 25 August 2004 (25.08.2004)	
Applicant's or agent's file reference 21812WO	**IMPORTANT NOTIFICATION**
International application No. PCT/EP2004/007288	International filing date (day/month/year) 01 July 2004 (01.07.2004)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 02 July 2003 (02.07.2003)
Applicant DSM IP ASSETS B.V. et al	

1. By means of this Form, which replaces any previously issued notification concerning submission or transmittal of priority documents, the applicant is hereby notified of the date of receipt by the International Bureau of the priority document(s) relating to all earlier application(s) whose priority is claimed. Unless otherwise indicated by the letters "NR", in the right-hand column or by an asterisk appearing next to a date of receipt, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).

2. (If applicable) The **letters "NR"** appearing in the right-hand column denote **a priority document which, on the date of mailing of this Form, had not yet been received by the International Bureau** under Rule 17.1(a) or (b). Where, under Rule 17.1(a), the priority document must be submitted by the applicant to the receiving Office or the International Bureau, but the applicant fails to submit the priority document within the applicable time limit under that Rule, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

3. (If applicable) An **asterisk(*)** appearing next to a date of receipt, in the right-hand column, denotes **a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b)** (the priority document was received after the time limit prescribed in Rule 17.1(a) or the request to prepare and transmit the priority document was submitted to the receiving Office after the applicable time limit under Rule 17.1(b)). Even though the priority document was not furnished in compliance with Rule 17.1(a) or (b), the International Bureau will nevertheless transmit a copy of the document to the designated Offices, for their consideration. In case such a copy is not accepted by the designated Office as priority document, Rule 17.1(c) provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
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